

REPLACEMENT SHEET

1/32

Figure 1

M K H L W F F L L L V A A P R
GAC ATG AAA CAC CTG TGG TTC TTC CTC CTC CTG GTG GCA GCC CCC AGA

+1 10
W V L S Q V Q L Q E A G P G L V
TGG GTC TTG TCC CAG GTG CAG CTG CAG GAG GCG GGC CCA GGA CTG GTG

20
K P S E T L S L T C S V S G G S
AAG CCT TCG GAG ACC CTG TCC CTC ACC TGC AGT GTC TCT GGT GGC TCC

30 40
I S G D Y Y W F W I R Q S P G K
ATC AGC GGT GAC TAT TAT TGG TTC TGG ATC CGC CAG TCC CCA GGG AAG

50 60
G L E W I G Y I Y G S G G G T N
GGA CTG GAG TGG ATC GGC TAC ATC TAT GGC AGT GGT GGG GGC ACC AAT

70
Y N P S L N N R V S I S I D T S
TAC AAT CCC TCC CTC AAC AAT CGA GTC TCC ATT TCA ATA GAC ACG TCC

80 90
K N L F S L K L R S V T A A D T
AAG AAC CTC TTC TCC CTG AAA CTG AGG TCT GTG ACC GCC GCG GAC ACG

100
A V Y Y C A S N I L K Y L H W L
GCC GTC TAT TAC TGT GCG AGT AAT ATA TTG AAA TAT CTT CAC TGG TTA

110 120
L Y W G Q G V L V T V S S
TTA TAC TGG GGC CAG GGA GTC CTG GTC ACC GTC TCC TCA (SEQ ID NO:1)

REPLACEMENT SHEET

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Figure 2

M A W A L L L L G L L A H F T
ACC ATG GCC TGG GCT CTG CTG CTC CTC GGC CTC CTT GCT CAC TTT ACA

+1 10
D S A A S Y E L S Q P R S V S V
GAC TCT GCG GCC TCC TAT GAG TTG AGT CAG CCT CGC TCA GTG TCC GTG

20
S P G Q T A G F T C G G D N V G
TCC CCA GGA CAG ACG GCC GGG TTC ACC TGT GGG GGA GAC AAC GTT GGA

30 40
R K S V Q W Y Q Q K P P Q A P V
AGG AAA AGT GTA CAG TGG TAC CAG CAG AAG CCA CCG CAG GCC CCT GTG

50 60
L V I Y A D S E R P S G I P A R
CTG GTC ATC TAT GCT GAC AGC GAA CGG CCC TCA GGG ATC CCT GCG CGA

70
F S G S N S G N T A T L T I S G
TTC TCT GGC TCC AAC TCA GGG AAC ACC GCC ACC CTG ACC ATC AGC GGG

80 90
V E A G D E A D Y Y C Q V W D S
GTC GAG GCC GGG GAT GAG GCT GAC TAT TAC TGT CAG GTG TGG GAC AGT

100
T A D H W V F G G G T R L T V L
ACT GCT GAT CAT TGG GTC TTC GGC GGA GGG ACC CGG CTG ACC GTC CTA

109
G
GGT (SEQ ID NO:3)

REPLACEMENT SHEET

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Figure 3

Frame 1 Met Ala Trp Ala Leu Leu Leu Leu Gly Leu Leu Ala His Phe Thr Asp Ser Ala Ala
 ATG GCC TGG GCT CTG CTG CTC CTC GGC CTC CTT GCT CAC TTT ACA GAC TCT GCG GCC
 9 18 27 36 45 54

Ser Tyr Glu Leu Ser Gln Pro Arg Ser Val Ser Val Ser Pro Gly Gln Thr Ala Gly Phe Thr
 TCC TAT GAG TTG AGT CAG CCT CGC TCA GTG TCC GTG TCC CCA GGA CAG ACG GCC GGG TTC ACC
 66 75 84 93 102 111 120

Cys Gly Gly Asp Asn Val Gly Arg Lys Ser Val Gln Trp Tyr Gln Gln Lys Pro Pro Gln Ala
 TGT GGG GGA GAC AAC GTT GGA AGG AAA AGT GTA CAG TGG TAC CAG CAG AAG CCA CCG CAG GCC
 129 138 147 156 165 174 183

Pro Val Leu Val Ile Tyr Ala Asp Ser Glu Arg Pro Ser Gly Ile Pro Ala Arg Phe Ser Gly
 CCT GTG CTG GTC ATC TAT GCT GAC AGC GAA CGG CCC TCA GGG ATC CCT GCG CGA TTC TCT GGC
 192 201 210 219 228 237 246

Ser Asn Ser Gly Asn Thr Ala Thr Leu Thr Ile Ser Gly Val Glu Ala Gly Asp Glu Ala Asp
 TCC AAC TCA GGG AAC ACC GCC ACC CTG ACC ATC AGC GGG GTC GAG GCC GGG GAT GAG GCT GAC
 255 264 273 282 291 300 309

Tyr Tyr Cys Gln Val Trp Asp Ser Thr Ala Asp His Trp Val Phe Gly Gly Gly Thr Arg Leu
 TAT TAC TGT CAG GTG TGG GAC AGT ACT GCT GAT CAT TGG GTC TTC GGC GGA GGG ACC CGG CTG
 318 327 336 345 354 363 372

Thr Val Leu Gly Gln Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro Ser Ser Glu Glu
 ACC GTC CTA GGT CAG CCC AAG GCT GCC CCC TCG GTC ACT CTG TTC CCG CCC TCC TCT GAG GAG
 381 390 399 408 417 426 435

Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile Ser Asp Phe Tyr Pro Gly Ala Val Thr
 CTT CAA GCC AAC AAG GCC ACA CTG GTG TGT CTC ATA AGT GAC TTC TAC CCG GGA GCC GTG ACA
 444 453 462 471 480 489 498

Val Ala Trp Lys Ala Asp Ser Ser Pro Val Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys
 GTG GCC TGG AAG GCA GAT AGC AGC CCC GTC AAG GCG GGA GTG GAG ACC ACC ACA CCC TCC AAA
 507 516 525 534 543 552 561

Gln Ser Asn Asn Lys Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln Trp Lys Ser
 CAA AGC AAC AAC AAG TAC GCG GCC AGC AGC TAC CTG AGC CTG ACG CCT GAG CAG TGG AAG TCC
 570 579 588 597 606 615 624

His Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser Thr Val Glu Lys Thr Val Ala Pro
 CAC AGA AGC TAC AGC TGC CAG GTC ACG CAT GAA GGG AGC ACC GTG GAG AAG ACA GTG GCC CCT
 633 642 651 660 669 678 687

Thr Glu Cys Ser TER
 ACA GAA TGT TCA TGA (SEQ ID NO:5)

REPLACEMENT SHEET

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Figure 4

Frame 1 Met Lys His Leu Trp Phe Phe Leu Leu Leu Val Ala Ala Pro Arg Trp Val Leu Ser
 ATG AAA CAC CTG TGG TTC TTC CTC CTC CTG GTG GCA GCC CCC AGA TGG GTC TTG TCC
 9 18 27 36 45 54

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu Thr Leu Ser Leu Thr
 CAG GTG CAG CTG CAG GAG TCG GGC CCA GGA CTG GTG AAG CCT TCG GAG ACC CTG TCC CTC ACC
 66 75 84 93 102 111 120

Cys Ser Val Ser Gly Gly Ser Ile Ser Gly Asp Tyr Tyr Trp Phe Trp Ile Arg Gln Ser Pro
 TGC AGT GTC TCT GGT GGC TCC ATC AGC GGT GAC TAT TAT TGG TTC TGG ATC CGC CAG TCC CCA
 129 138 147 156 165 174 183

Gly Lys Gly Leu Glu Trp Ile Gly Tyr Ile Tyr Gly Ser Gly Gly Gly Thr Asn Tyr Asn Pro
 GGG AAG GGA CTG GAG TGG ATC GGC TAC ATC TAT GGC AGT GGT GGG GGC ACC AAT TAC AAT CCC
 192 201 210 219 228 237 246

Ser Leu Asn Asn Arg Val Ser Ile Ser Ile Asp Thr Ser Lys Asn Leu Phe Ser Leu Lys Leu
 TCC CTC AAC AAT CGA GTC TCC ATT TCA ATA GAC ACG TCC AAG AAC CTC TTC TCC CTG AAA CTG
 255 264 273 282 291 300 309

Arg Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Ser Asn Ile Leu Lys Tyr Leu
 AGG TCT GTG ACC GCC GCG GAC ACG GCC GTC TAT TAC TGT GCG AGT AAT ATA TTG AAA TAT CTT
 318 327 336 345 354 363 372

His Trp Leu Leu Tyr Trp Gly Gln Gly Val Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
 CAC TGG TTA TTA TAC TGG GGC CAG GGA GTC CTG GTC ACC GTC TCC TCA GCT AGC ACC AAG GGC
 381 390 399 408 417 426 435

Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly
 CCA TCC GTC TTC CCC CTG GCG CCC TGC TCC AGG AGC ACC TCC GAG AGC ACA GCC GCC CTG GGC
 444 453 462 471 480 489 498

Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr
 TGC CTG GTC AAG GAC TAC TTC CCC GAA CCG GTG ACG GTG TCG TGG AAC TCA GGC GCC CTG ACC
 507 516 525 534 543 552 561

Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val
 AGC GGC GTG CAC ACC TTC CCG GCT GTC CTA CAG TCC TCA GGA CTC TAC TCC CTC AGC AGC GTG
 570 579 588 597 606 615 624

Val Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His Lys Pro
 GTG ACC GTG CCC TCC AGC AGC TTG GGC ACG AAG ACC TAC ACC TGC AAC GTA GAT CAC AAG CCC
 633 642 651 660 669 678 687

Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro Ser Cys Pro

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Figure 4 (Continued)

AGC AAC ACC AAG GTG GAC AAG AGA GTT GAG TCC AAA TAT GGT CCC CCA TGC CCA TCA TGC CCA
696 705 714 723 732 741 750

Ala Pro Glu Phe Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
GCA CCT GAG TTC CTG GGG GGA CCA TCA GTC TTC CTG TTC CCC CCA AAA CCC AAG GAC ACT CTC
759 768 777 786 795 804 813

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro Glu
ATG ATC TCC CGG ACC CCT GAG GTC ACG TGC GTG GTG GTG GAC GTG AGC CAG GAA GAC CCC GAG
822 831 840 849 858 867 876

Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
GTC CAG TTC AAC TGG TAC GTG GAT GGC GTG GAG GTG CAT AAT GCC AAG ACA AAG CCG CGG GAG
885 894 903 912 921 930 939

Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
GAG CAG TTC AAC AGC ACG TAC CGT GTG GTC AGC GTC CTC ACC GTC CTG CAC CAG GAC TGG CTG
948 957 966 975 984 993 1002

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr
AAC GGC AAG GAG TAC AAG TGC AAG GTC TCC AAC AAA GGC CTC CCG TCC TCC ATC GAG AAA ACC
1011 1020 1029 1038 1047 1056 1065

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu
ATC TCC AAA GCC AAA GGG CAG CCC CGA GAG CCA CAG GTG TAC ACC CTG CCC CCA TCC CAG GAG
1074 1083 1092 1101 1110 1119 1128

Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
GAG ATG ACC AAG AAC CAG GTC AGC CTG ACC TGC CTG GTC AAA GGC TTC TAC CCC AGC GAC ATC
1137 1146 1155 1164 1173 1182 1191

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
GCC GTG GAG TGG GAG AGC AAT GGG CAG CCG GAG AAC AAC TAC AAG ACC ACG CCT CCC GTG CTG
1200 1209 1218 1227 1236 1245 1254

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu
GAC TCC GAC GGC TCC TTC TTC CTC TAC AGC AGG CTA ACC GTG GAC AAG AGC AGG TGG CAG GAG
1263 1272 1281 1290 1299 1308 1317

Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
GGG AAT GTC TTC TCA TGC TCC GTG ATG CAT GAG GCT CTG CAC AAC CAC TAC ACA CAG AAG AGC
1326 1335 1344 1353 1362 1371 1380

Leu Ser Leu Ser Leu Gly Lys TER
CTC TCC CTG TCT CTG GGT AAA TGA (SEQ ID NO:7)
1389 1398

REPLACEMENT SHEET

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Figure 5

Frame 1 Met Lys His Leu Trp Phe Phe Leu Leu Leu Val Ala Ala Pro Arg Trp Val Leu Ser
 ATG AAA CAC CTG TGG TTC TTC CTC CTC CTG GTG GCA GCC CCC AGA TGG GTC TTG TCC
 9 18 27 36 45 54

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu Thr Leu Ser Leu Thr
 CAG GTG CAG CTG CAG GAG TCG GGC CCA GGA CTG GTG AAG CCT TCG GAG ACC CTG TCC CTC ACC
 66 75 84 93 102 111 120

Cys Ser Val Ser Gly Gly Ser Ile Ser Gly Asp Tyr Tyr Trp Phe Trp Ile Arg Gln Ser Pro
 TGC AGT GTC TCT GGT GGC TCC ATC AGC GGT GAC TAT TAT TGG TTC TGG ATC CGC CAG TCC CCA
 129 138 147 156 165 174 183

Gly Lys Gly Leu Glu Trp Ile Gly Tyr Ile Tyr Gly Ser Gly Gly Gly Thr Asn Tyr Asn Pro
 GGG AAG GGA CTG GAG TGG ATC GGC TAC ATC TAT GGC AGT GGT GGG GGC ACC AAT TAC AAT CCC
 192 201 210 219 228 237 246

Ser Leu Asn Asn Arg Val Ser Ile Ser Ile Asp Thr Ser Lys Asn Leu Phe Ser Leu Lys Leu
 TCC CTC AAC AAT CGA GTC TCC ATT TCA ATA GAC ACG TCC AAG AAC CTC TTC TCC CTG AAA CTG
 255 264 273 282 291 300 309

Arg Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Ser Asn Ile Leu Lys Tyr Leu
 AGG TCT GTG ACC GCC GCG GAC ACG GCC GTC TAT TAC TGT GCG AGT AAT ATA TTG AAA TAT CTT
 318 327 336 345 354 363 372

His Trp Leu Leu Tyr Trp Gly Gln Gly Val Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
 CAC TGG TTA TTA TAC TGG GGC CAG GGA GTC CTG GTC ACC GTC TCC TCA GCT AGC ACC AAG GGG
 381 390 399 408 417 426 435

Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly
 CCA TCC GTC TTC CCC CTG GCG CCC TGC TCC AGG AGC ACC TCC GAG AGC ACA GCC GCC CTG GGC
 444 453 462 471 480 489 498

Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr
 TGC CTG GTC AAG GAC TAC TTC CCC GAA CCG GTG ACG GTG TCG TGG AAC TCA GGC GCC CTG ACC
 507 516 525 534 543 552 561

Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val
 AGC GGC GTG CAC ACC TTC CCG GCT GTC CTA CAG TCC TCA GGA CTC TAC TCC CTC AGC AGC GTG
 570 579 588 597 606 615 624

Val Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His Lys Pro
 GTG ACC GTG CCC TCC AGC AGC TTG GGC ACG AAG ACC TAC ACC TGC AAC GTA GAT CAC AAG CCC
 633 642 651 660 669 678 687

Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro Ser Cys Pro

REPLACEMENT SHEET

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Figure 5 (Continued)

AGC AAC ACC AAG GTG GAC AAG AGA GTT GAG TCC AAA TAT GGT CCC CCA TGC CCA TCA TGC CCA
696 705 714 723 732 741 750

Ala Pro Glu Phe Glu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
GCA CCT GAG TTC GAG GGG GGA CCA TCA GTC TTC CTG TTC CCC CCA AAA CCC AAG GAC ACT CTC
759 768 777 786 795 804 813

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro Glu
ATG ATC TCC CGG ACC CCT GAG GTC ACG TGC GTG GTG GTG GAC GTG AGC CAG GAA GAC CCC GAG
822 831 840 849 858 867 876

Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
GTC CAG TTC AAC TGG TAC GTG GAT GGC GTG GAG GTG CAT AAT GCC AAG ACA AAG CCG CGG GAG
885 894 903 912 921 930 939

Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
GAG CAG TTC AAC AGC ACG TAC CGT GTG GTC AGC GTC CTC ACC GTC CTG CAC CAG GAC TGG CTG
948 957 966 975 984 993 1002

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr
AAC GGC AAG GAG TAC AAG TGC AAG GTC TCC AAC AAA GGC CTC CCG TCC TCC ATC GAG AAA ACC
1011 1020 1029 1038 1047 1056 1065

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu
ATC TCC AAA GCC AAA GGG CAG CCC CGA GAG CCA CAG GTG TAC ACC CTG CCC CCA TCC CAG GAG
1074 1083 1092 1101 1110 1119 1128

Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
GAG ATG ACC AAG AAC CAG GTC AGC CTG ACC TGC CTG GTC AAA GGC TTC TAC CCC AGC GAC ATC
1137 1146 1155 1164 1173 1182 1191

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
GCC GTG GAG TGG GAG AGC AAT GGG CAG CCG GAG AAC AAC TAC AAG ACC ACG CCT CCC GTG CTG
1200 1209 1218 1227 1236 1245 1254

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu
GAC TCC GAC GGC TCC TTC TTC CTC TAC AGC AGG CTA ACC GTG GAC AAG AGC AGG TGG CAG GAG
1263 1272 1281 1290 1299 1308 1317

Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
GGG AAT GTC TTC TCA TGC TCC GTG ATG CAT GAG GCT CTG CAC AAC CAC TAC ACA CAG AAG AGC
1326 1335 1344 1353 1362 1371 1380

Leu Ser Leu Ser Leu Gly Lys TER

CTC TCC CTG TCT CTG GGT AAA TGA (SEQ ID NO:9)
1389 1398

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Figure 6

| | | | | | | | | | | | | | | | | | | | |
|---------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Frame 1 | Met | Lys | His | Leu | Trp | Phe | Phe | Leu | Leu | Leu | Val | Ala | Ala | Pro | Arg | Trp | Val | Leu | Ser |
| | ATG | AAA | CAC | CTG | TGG | TTC | TTC | CTC | CTC | CTG | GTG | GCA | GCC | CCC | AGA | TGG | GTC | TTG | TCC |
| | | | 9 | | | 18 | | | 27 | | 36 | | | | 45 | | 54 | | |

| | | | | | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Gln | Val | Gln | Leu | Gln | Glu | Ser | Gly | Pro | Gly | Leu | Val | Lys | Pro | Ser | Glu | Thr | Leu | Ser | Leu | Thr |
| CAG | GTG | CAG | CTG | CAG | GAG | TCG | GGC | CCA | GGA | CTG | GTG | AAG | CCT | TCG | GAG | ACC | CTG | TCC | CTC | ACC |
| | 66 | | | 75 | | | 84 | | | 93 | | | 102 | | | 111 | | | 120 | |

| | | | | | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Cys | Ser | Val | Ser | Gly | Gly | Ser | Ile | Ser | Gly | Asp | Tyr | Tyr | Trp | Phe | Trp | Ile | Arg | Gln | Ser | Pro |
| TGC | AGT | GTC | TCT | GGT | GGC | TCC | ATC | AGC | GGT | GAC | TAT | TAT | TGG | TTC | TGG | ATC | CGC | CAG | TCC | CCA |
| | 129 | | | 138 | | | 147 | | | 156 | | | 165 | | | 174 | | | 183 | |

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|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Gly | Lys | Gly | Leu | Glu | Trp | Ile | Gly | Tyr | Ile | Tyr | Gly | Ser | Gly | Gly | Gly | Thr | Asn | Tyr | Asn | Pro |
| GGG | AAG | GGA | CTG | GAG | TGG | ATC | GGC | TAC | ATC | TAT | GGC | AGT | GGT | GGG | GGC | ACC | AAT | TAC | AAT | CCC |
| | 192 | | | 201 | | | 210 | | | 219 | | | 228 | | | 237 | | | 246 | |

| | | | | | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Ser | Leu | Asn | Asn | Arg | Val | Ser | Ile | Ser | Ile | Asp | Thr | Ser | Lys | Asn | Leu | Phe | Ser | Leu | Lys | Leu |
| TCC | CTC | AAC | AAT | CGA | GTC | TCC | ATT | TCA | ATA | GAC | ACG | TCC | AAG | AAC | CTC | TTC | TCC | CTG | AAA | CTG |
| | 255 | | | 264 | | | 273 | | | 282 | | | 291 | | | 300 | | | 309 | |

| | | | | | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Arg | Ser | Val | Thr | Ala | Ala | Asp | Thr | Ala | Val | Tyr | Tyr | Cys | Ala | Ser | Asn | Ile | Leu | Lys | Tyr | Leu |
| AGG | TCT | GTG | ACC | GCC | GCG | GAC | ACG | GCC | GTC | TAT | TAC | TGT | GCG | AGT | AAT | ATA | TTG | AAA | TAT | CTT |
| | 318 | | | 327 | | | 336 | | | 345 | | | 354 | | | 363 | | | 372 | |

| | | | | | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| His | Trp | Leu | Leu | Tyr | Trp | Gly | Gln | Gly | Val | Leu | Val | Thr | Val | Ser | Ser | Ala | Ser | Thr | Lys | Gly |
| CAC | TGG | TTA | TTA | TAC | TGG | GGC | CAG | GGA | GTC | CTG | GTC | ACC | GTC | TCC | TCA | GCT | AGC | ACC | AAG | GGG |
| | 381 | | | 390 | | | 399 | | | 408 | | | 417 | | | 426 | | | 435 | |

| | | | | | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Pro | Ser | Val | Phe | Pro | Leu | Ala | Pro | Cys | Ser | Arg | Ser | Thr | Ser | Glu | Ser | Thr | Ala | Ala | Leu | Gly |
| CCA | TCC | GTC | TTC | CCC | CTG | GCG | CCC | TGC | TCC | AGG | AGC | ACC | TCC | GAG | AGC | ACA | GCC | GCC | CTG | GGC |
| | 444 | | | 453 | | | 462 | | | 471 | | | 480 | | | 489 | | | 498 | |

| | | | | | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Cys | Leu | Val | Lys | Asp | Tyr | Phe | Pro | Glu | Pro | Val | Thr | Val | Ser | Trp | Asn | Ser | Gly | Ala | Leu | Thr |
| TGC | CTG | GTC | AAG | GAC | TAC | TTC | CCC | GAA | CCG | GTG | ACG | GTG | TCG | TGG | AAC | TCA | GGC | GCC | CTG | ACC |
| | 507 | | | 516 | | | 525 | | | 534 | | | 543 | | | 552 | | | 561 | |

| | | | | | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Ser | Gly | Val | His | Thr | Phe | Pro | Ala | Val | Leu | Gln | Ser | Ser | Gly | Leu | Tyr | Ser | Leu | Ser | Ser | Val |
| AGC | GGC | GTG | CAC | ACC | TTC | CCG | GCT | GTC | CTA | CAG | TCC | TCA | GGA | CTC | TAC | TCC | CTC | AGC | AGC | GTG |
| | 570 | | | 579 | | | 588 | | | 597 | | | 606 | | | 615 | | | 624 | |

| | | | | | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Val | Thr | Val | Pro | Ser | Ser | Ser | Leu | Gly | Thr | Lys | Thr | Tyr | Thr | Cys | Asn | Val | Asp | His | Lys | Pro |
| GTG | ACC | GTG | CCC | TCC | AGC | AGC | TTG | GGC | ACG | AAG | ACC | TAC | ACC | TGC | AAC | GTA | GAT | CAC | AAG | CCC |
| | 633 | | | 642 | | | 651 | | | 660 | | | 669 | | | 678 | | | 687 | |

| | | | | | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Ser | Asn | Thr | Lys | Val | Asp | Lys | Arg | Val | Glu | Ser | Lys | Tyr | Gly | Pro | Pro | Cys | Pro | Pro | Cys | Pro |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|

REPLACEMENT SHEET

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Figure 6 (Continued)

| | | | | | | | | |
|---|---|------|------|----------------|------|------|------|------|
| AGC AAC ACC AAG GTG GAC AAG AGA GTT GAG TCC AAA TAT GGT CCC CCA TGC CCA CCA TGC CCA | 696 | 705 | 714 | 723 | 732 | 741 | 750 | |
| Ala Pro Glu Phe Glu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu | GCA CCT GAG TTC GAG GGG GGA CCA TCA GTC TTC CTG TTC CCC CCA AAA CCC AAG GAC ACT CTC | 759 | 768 | 777 | 786 | 795 | 804 | 813 |
| Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro Glu | ATG ATC TCC CGG ACC CCT GAG GTC ACG TGC GTG GTG GTG GAC GTG AGC CAG GAA GAC CCC GAG | 822 | 831 | 840 | 849 | 858 | 867 | 876 |
| Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu | GTC CAG TTC AAC TGG TAC GTG GAT GGC GTG GAG GTG CAT AAT GCC AAG ACA AAG CCG CGG GAG | 885 | 894 | 903 | 912 | 921 | 930 | 939 |
| Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu | GAG CAG TTC AAC AGC ACG TAC CGT GTG GTC AGC GTC CTC ACC GTC CTG CAC CAG GAC TGG CTG | 948 | 957 | 966 | 975 | 984 | 993 | 1002 |
| Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr | AAC GGC AAG GAG TAC AAG TGC AAG GTC TCC AAC AAA GGC CTC CCG TCC TCC ATC GAG AAA ACC | 1011 | 1020 | 1029 | 1038 | 1047 | 1056 | 1065 |
| Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu | ATC TCC AAA GCC AAA GGG CAG CCC CGA GAG CCA CAG GTG TAC ACC CTG CCC CCA TCC CAG GAG | 1074 | 1083 | 1092 | 1101 | 1110 | 1119 | 1128 |
| Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile | GAG ATG ACC AAG AAC CAG GTC AGC CTG ACC TGC CTG GTC AAA GGC TTC TAC CCC AGC GAC ATC | 1137 | 1146 | 1155 | 1164 | 1173 | 1182 | 1191 |
| Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu | GCC GTG GAG TGG GAG AGC AAT GGG CAG CCG GAG AAC AAC TAC AAG ACC ACG CCT CCC GTG CTG | 1200 | 1209 | 1218 | 1227 | 1236 | 1245 | 1254 |
| Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu | GAC TCC GAC GGC TCC TTC TTC CTC TAC AGC AGG CTA ACC GTG GAC AAG AGC AGG TGG CAG GAG | 1263 | 1272 | 1281 | 1290 | 1299 | 1308 | 1317 |
| Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser | GGG AAT GTC TTC TCA TGC TCC GTG ATG CAT GAG GCT CTG CAC AAC CAC TAC ACA CAG AAG AGC | 1326 | 1335 | 1344 | 1353 | 1362 | 1371 | 1380 |
| Leu Ser Leu Ser Leu Gly Lys TER | CTC TCC CTG TCT CTG GGT AAA TGA | 1389 | 1398 | (SEQ ID NO:11) | | | | |

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Figure 7-1

Primers for the Amplification of Monkey Immunoglobulin Heavy Chain Variable Regions5' Sense' PrimersA. Human or Monkey heavy chain early leader sequence primers with Sall site

| | | |
|------------------|--|----------------|
| V _H 1 | 5' ACTAAGTCGACATGGACTGGACCTTGG 3' | (SEQ ID NO:13) |
| V _H 2 | 5' ACTAAGTCGACATGGACATACCTTTGTTCCAC 3' | (SEQ ID NO:14) |
| V _H 3 | 5' ACTAAGTCGACATGGAGTTTGGGCTGAGC 3' | (SEQ ID NO:15) |
| V _H 4 | 5' ACTAAGTCGACATGAAACACCTGTGGTTCTT 3' | (SEQ ID NO:16) |
| V _H 5 | 5' ACTAAGTCGACATGGGGTCAACCGCCATCCT 3' | (SEQ ID NO:17) |
| V _H 6 | 5' ACTAAGTCGACATGTCTGTCTCCTTCCTCAT 3' | (SEQ ID NO:18) |

B. Human or Monkey heavy chain late leader sequence primers with Mlu I site

| | | |
|------------------|---|----------------|
| V _H 1 | 5' G GCA GCA GC (CT) <u>ACG CGT</u> GCC CAC TCC GAG GT 3' | (SEQ ID NO:19) |
| V _H 2 | 5' G ACC GTC CCG <u>ACG CGT</u> GT (TC) TTG TCC CAG GT 3' | (SEQ ID NO:20) |
| V _H 3 | 5' GCT ATT TTC <u>ACG CGT</u> GTC CAG TGT GAG 3' | (SEQ ID NO:21) |
| V _H 4 | 5' GCG GCT CCC <u>ACG CGT</u> GTC CTG TCC CAG 3' | (SEQ ID NO:22) |
| V _H 5 | 5' G GCT GTT CTC <u>ACG CGT</u> GTC TGT GCC GAG GT 3' | (SEQ ID NO:23) |

Figure 7-1 (Continued)

C. Human or Monkey framework 1 sequence primers with *Xho* / site

| | | |
|-----------------------|---------------------------------------|----------------|
| V _H 1,3a,5 | ⁺¹ CAGGTGCAGCTGCTCGAGTCTGG | (SEQ ID NO:24) |
| V _H 2 | ⁺¹ CAGGTCAACTTACTCGAGTCTGG | (SEQ ID NO:25) |
| V _H 3b | ⁺¹ GAGGTGCAGCTGCTCGAGTCTGG | (SEQ ID NO:26) |
| V _H 4 | ⁺¹ CAGGTGCAGCTGCTCGAGTCGGG | (SEQ ID NO:27) |
| V _H 6 | ⁺¹ CAGGTACAGCTGCTCGAGTCAGG | (SEQ ID NO:28) |

3' Anti-Sense' Primers

A. Human or Monkey heavy chain constant region primers anti-sense strand with *Nhe* 1 site

| | | |
|--------------------|--|----------------|
| IgG ₁₋₄ | ⁺¹¹⁸ 5' GGC GGA TGC GCT AGC TGA GGA GAC GG 3' | (SEQ ID NO:29) |
| | <div>Nhe 1</div> | |

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Figure 7-2

Primers for the Amplification of Monkey Immunoglobulin Light Chain Variable Regions5' Sense' PrimersA. Human or Monkey kappa light chain early leader primers with Bgl II site

1. 5' ATCACAGATCTCTCACCATGGTGTTCAGACCCAGGTC 3' (SEQ ID NO:30)
2. 5' ATCACAGATCTCTCACCATGG (GA) G (AT) CCCC (TA) GC (TG) CAGCT 3' (SEQ ID NO:31)
3. 5' ATCACAGATCTCTCACCATGGACATGAGGTCCTCCGCTCAG 3' (SEQ ID NO:32)
4. 5' ATCACAGATCTCTCACCATGGACAC (GAC) AGGGCCCCCACTCAG 3' (SEQ ID NO:33)

B. Human or Monkey lambda light chain early leader primers with Bgl II site

1. 5' ATCACAGATCTCTCACCATGGCCCTGGGCTCTGTGCTCC 3' (SEQ ID NO:34)
2. 5' ATCACAGATCTCTCACCATGGCCCTGGGCTCCACTACTTC 3' (SEQ ID NO:35)
3. 5' ATCACAGATCTCTCACCATGACCTGCTCCCTCTCCTCC 3' (SEQ ID NO:36)
4. 5' ATCACAGATCTCTCACCATGGCCCTGGACTCCTCTCTTTC 3' (SEQ ID NO:37)
5. 5' ATCACAGATCTCTCACCATGACTTGGACCCCACTCCTC 3' (SEQ ID NO:38)

Figure 7-2 (Continued)

A. Human or Monkey kappa light chain constant region primer anti-sense strand with *Kpn* 1 and *Bsi*W1 sites

C_{Kappa}

+108
5' CCG TTT GAT TTC CAG CTT GGT ACC TCC ACC GAA CGT 3' +97
Kpn 1

+112
5' TGC AGC ATC CGT ACG TTT GAT TTC CAG CTT 3' +103
BsiW1

(SEQ ID NO:39)

(SEQ ID NO:40)

B. Human or Monkey lambda light chain constant region primer anti-sense strand with *Kpn* I, *Hind* III and *Avr* II sites

C_{Lambda}

+107 5' ACC TAG GAC GGT AAG CTT GGT ACC TCC GCC 3' +99 (SEQ ID NO:41)

Hind III Kpn 1

+107 5' ACC TAG GAC GGT CA (C/G) (C/G) TT GGT ACC TCC GCC GAA CAC 3' +97 (SEQ ID NO:42)

Kpn 1

+110 5' CTT GGG CTG ACC TAG GAC GGT GAG CCG 3' +102 (SEQ ID NO:43)

Avr II

Figure 8

A. Heavy chain variable region:

| | | |
|-----|----------------------------|----------------|
| VH1 | 5' CCATGGACTGGACCTGG 3' | (SEQ ID NO:44) |
| VH2 | 5' ATGGACATACTTTGTTCCAC 3' | (SEQ ID NO:45) |
| VH3 | 5' CCATGGAGTTTGGGCTGAGC 3' | (SEQ ID NO:46) |
| VH4 | 5' ATGAAACACCTGTGGTTCTT 3' | (SEQ ID NO:47) |
| VH5 | 5' ATGGGTCAACCGCCATCCT 3' | (SEQ ID NO:48) |
| VH6 | 5' ATGTCGTCTCCTTCCTCAT 3' | (SEQ ID NO:49) |

B. Heavy chain constant region anti-sense strand:

| | | |
|--------------------|--|----------------|
| IgM | ⁺¹¹⁹ 5' T TGG GGC GGA TGC ACT 3' | (SEQ ID NO:50) |
| IgG ₁₋₄ | ⁺¹¹⁹ 5' GA TGG GCC CTT GGT GGA 3' | (SEQ ID NO:51) |

C. Light chain variable region:

| | | |
|--------|--|----------------|
| Kappa | ⁺⁴ 5' G ATG ACC CAG TCT CCA (G/T)CC TC 3' | (SEQ ID NO:52) |
| Lambda | ⁻⁹ 5' CTC A(C/T)T(T/C) (G/A)C TGC(A/C)CA GGG TCC 3' | (SEQ ID NO:53) |

D. Light chain constant region anti-sense strands:

| | | |
|--------|---|----------------|
| Kappa | ⁺¹¹⁵ 5' AA GAC AGA TGG TGC AGC CA 3' | (SEQ ID NO:54) |
| Lambda | ⁺¹¹⁸ 5' G GAA CAG AGT GAC CGA GGG G 3' | (SEQ ID NO:55) |

Figure 16

PCR Primers for Human $\gamma 4$ Constant Region

1) IDEC 462 3' PCR Primer

5' GGGG GGA TCC TCA TTT ACC CAG AGA CAG GG 3' (SEQ ID NO:56)
 BamH I

2) IDEC 479 5' PCR Primer

5' GGGG GCT AGC ACC AAG GGC CCA TCC GTC TTC 3' (SEQ ID NO:57)
 Nhe I

PCR Mutagenesis of Human $\gamma 4$

3) IDEC 698 3' PCR Primer

5' CCG GGA GAT CAT GAG AGT GTC CTT GGG TTT TGG GGG GAA CAG GAA GAC
 BspH I
 TGA TGG TCC CCC CTC GAA CTC AGG TGC TGG GCA TGG TGG GCA TGG GGG 3' (SEQ ID NO:58)
 Glu Pro

4) Midland GE212 5' PCR Primer

5' TCC TCA GCT AGC ACC AAG GGG CCA TCC 3' (SEQ ID NO:59)
 Nhe I
 Destroys Apa I site

REPLACEMENT SHEET

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Figure 17

Frame 1 Met Lys His Leu Trp Phe Phe Leu Leu Leu Val Ala Ala Pro Arg Trp Val Leu Ser
 ATG AAA CAC CTG TGG TTC TTC CTC CTC CTG GTG GCA GCC CCC AGA TGG GTC TTG TCC
 9 18 27 36 45 54

+1

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu Thr Leu Ser Leu Thr
 CAG GTG CAG CTG CAG GAG TCG GGC CCA GGA CTG GTG AAG CCT TCG GAG ACC CTG TCC CTC ACC
 66 75 84 93 102 111 120

Cys Ser Val Ser Gly Gly Ser Ile Ser Gly Asp Tyr Tyr Trp Phe Trp Ile Arg Gln Ser Pro
 TGC AGT GTC TCT GGT GGC TCC ATC AGC GGT GAC TAT TAT TGG TTC TGG ATC CGC CAG TCC CCA
 129 138 147 156 165 174 183

Gly Lys Gly Leu Glu Trp Ile Gly Tyr Ile Tyr Gly Ser Gly Gly Gly Thr Asn Tyr Asn Pro
 GGG AAG GGA CTG GAG TGG ATC GGC TAC ATC TAT GGC AGT GGT GGG GGC ACC AAT TAC AAT CCC
 192 201 210 219 228 237 246

Ser Leu Asn Asn Arg Val Ser Ile Ser Ile Asp Thr Ser Lys Asn Leu Phe Ser Leu Lys Leu
 TCC CTC AAC AAT CGA GTC TCC ATT TCA ATA GAC ACG TCC AAG AAC CTC TTC TCC CTG AAA CTG
 255 264 273 282 291 300 309

Arg Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Ser Asn Ile Leu Lys Tyr Leu
 AGG TCT GTG ACC GCC GCG GAC ACG GCC GTC TAT TAC TGT GCG AGT AAT ATA TTG AAA TAT CTT
 318 327 336 345 354 363 372

His Trp Leu Leu Tyr Trp Gly Gln Gly Val Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
 CAC TGG TTA TTA TAC TGG GGC CAG GGA GTC CTG GTC ACC GTC TCC TCA GCT AGC ACC AAG GGG
 381 390 399 408 417 426 435

Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Ser Glu Ser Thr Ala Ala Leu Gly
 CCA TCC GTC TTC CCC CTG GCG CCC TGC TCC AGG AGC ACC TCC GAG AGC ACA GCC GCC CTG GGC
 444 453 462 471 480 489 498

Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr
 TGC CTG GTC AAG GAC TAC TTC CCC GAA CCG GTG ACG GTG TCG TGG AAC TCA GGC GCC CTG ACC
 507 516 525 534 543 552 561

Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val
 AGC GGC GTG CAC ACC TTC CCG GCT GTC CTA CAG TCC TCA GGA CTC TAC TCC CTC AGC AGC GTG
 570 579 588 597 606 615 624

Val Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His Lys Pro
 GTG ACC GTG CCC TCC AGC AGC TTG GGC ACG AAG ACC TAC ACC TGC AAC GTA GAT CAC AAG CCC
 633 642 651 660 669 678 687

Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro Pro Cys Pro

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Leu Ser Leu Ser Leu Gly Lys TER
CTC TCC CTG TCT CTG GGT AAA TGA (SEQ ID NO:11)
1389 1398